REMARKS

Part V Paragraph I. Novelty

In the First Written Opinion the Examiner found that Claims 5-8 and 12-16 met the PCT Article 33(2) criteria for novelty. However, the Examiner found that Claims 1-4 lack novelty because they were anticipated by **Inki et al.** (British J. Cancer 70:319-323 (1994)). The Examiner also determined that Claims 1-4 also lack novelty because they are anticipated by **Nackaerts et al.** (Int. J. Cancer 74:335-336 (1997). In addition Claims 1-4 and 9-11 were rejected for novelty over **Jalkanen et al.** (U.S. Patent No. 5,422,243). These same claims (1-4 and 9-11) were also rejected for lack of inventive step. However, the Examiner did not spell the basis for this rejection. Applicant assumes that **Nackaerts et al.** is the source of this rejection. However, if this supposition is incorrect, Applicant would appreciate an opportunity to address the alternate grounds for rejection.

Inki et al. and **Jalkanen et al.** both teach the production of antibodies to syndecan-1 whereas **Jalkanen et al.** also teaches the use of syndecan-1 antibodies for cancer determination. Neither of these references teach anything about glypicans. As pointed out on pages 1 and 2 of the current specification, although both syndecans and glypicans are both heparan sulfate proteoglycans, the two families of molecules have significantly different core proteins. Thus, they come from quite different genes and any finding about or use of one of these molecules would not necessarily apply to or render non-inventive a similar finding or use of the other. The claims have now been limited to only glypicans. This limitation eliminates the destruction of novelty due to **Inki et al.** or **Jalkanen et al.** Therefore, Applicant anticipates that negative findings based on these references will be withdrawn in the Final Written Report.

Nackaerts et al. uses antibodies both to syndecans and to glypicans. The amended claims no longer mention syndecans so **Nackaerts et al.** no longer destroys the novelty due to syndecans. Applicant respectfully contends that **Nackaerts et al.** does not destroy the novelty of using glypicans as a diagnostic agent for human cancer. Specifically, **Nackaerts et al.** teaches that the cancer cells studied either did not express glypican ("Reactions for syndecan-2 and -3 and glypican were always negative in these tumor cells"—third paragraph from bottom of col. 1, page 341) or the glypican expression did not correlate with degree of differentiation (*i.e.*, was not of diagnostic utility) ("Variable expression and no correlation with degree of differentiation were observed for syndecan-4 or glypican."—last line of page 339); ("Glypican and syndecan-

4 could be demonstrated in the human lung-tumor cells but without clear correlation with the differentiation of the cells"—middle of col. 2 on page 343). These results clearly indicate that neither glypican nor syndecan-1 could be used as cancer diagnostic agents. The negative use of glypican antibody in **Nackaerts et al.** does not destroy the novelty of the demonstrated positive use of glypican in the present study.

Part V Paragraph I. Inventive Step

As mentioned above, Applicant is uncertain of the basis for the finding of lack of inventive step for Claims 1-4 and 9-11. Since neither **Inki et al.** nor **Jalkanen et al.** teach use of gylpican antibodies, it would seem that these references cannot negate the inventive step of the invention as now claimed. In the absence of the present disclosure there is no prior art linkage between glypican and syndecan antibody diagnostic use. **Nackaerts et al.** does employ glypican antibodies, but as discussed above, this use is not as a diagnostic agent. To the contrary, **Nackaerts et al.** clearly demonstrates the lack of utility (in their system) of employing glypican detection as a cancer diagnostic. Thus, the references are either silent on glypican or actively teach away from the diagnostic use of glypican. Therefore, diagnostic cancer use of glypican does show the requisite inventive step.

Applicants believe that the above amendments and discussions have dealt with the Examiner's finding of laek of novelty for Claims 1-4 and 9-11 as well as lack of inventive step for these same claims. Applicant contends that all the claims are now novel and demonstrate a true inventive step as required by Article 33 (3) PCT and await the Examiner's affirmation of this contention. Any suggestions or recommendations on claim structure are appreciated, and the Examiner is respectfully requested to contact the undersigned with any such suggestions.

Respectfully submitted,

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CLAIMS

What Is Claimed Is:

1. A diagnostic agent for human cancer comprising a binding molecule that binds to glypican-1 and a reporting molecule attachable to the binding molecule whereby a detection method can detect the presence of the binding molecule by detecting the reporting molecule.

2. The diagnostic agent of Claim 1, wherein the binding molecule comprises an antibody.

3. The diagnostic agent of Claim 2, wherein the antibody is used to detect glypican-1 in a body fluid.

4. The diagnostic agent of Claim 2, wherein the antibody is used to image glypican-1.

5. A therapeutic agent for slowing growth of human cancer cells comprising a molecule that affects glypican-1 by one of binding to an extracellular region of glypican-1, cleaving an extracellular region of glypican-1 and suppressing expression of an extracellular region of glypican-1.

6. The therapeutic agent of Claim 5, wherein the molecule comprises an antibody the binds to the extracellular region of glypican-1.

7. The therapeutic agent of Claim 5, wherein the molecule comprises an enzyme that digests a portion of the extracellular region of glypican-1.

8. The therapeutic agent of Claim 5, wherein the molecule comprises a nucleic acid molecule that suppresses expression of the extracellular region of glypican-1.

9. A method for diagnosing human cancer comprising the steps of contacting a molecule that binds to glypican-1 with either a body fluid or body tissue, and detecting the molecule bound to glypican-1.

10. The method of Claim 9, wherein the binding molecule comprises an antibody.

11. The method of Claim 10, wherein the antibody is used to detect glypican-1.

12. The method of Claim 10, wherein the antibody is used to image glypican-1.

13. A method of slowing growth of human cancer cells comprising administering a molecule that affects glypican-1 by one of binding to an extracellular region of glypican-1, cleaving an extracellular region of glypican-1 and suppressing expression of an extracellular region of glypican-1.

14. The method of Claim 13, wherein the molecule comprises an antibody the binds to the extracellular region of glypican-1.

15. The method of Claim 13, wherein the molecule comprises an enzyme that digests a portion of the extracellular region of glypican-1.

16. The method of Claim 13, wherein the molecule comprises a nucleic acid molecule that suppresses expression of the extracellular region of glypican-1.